AUTHOR INDEX

Andreu, J. M. 191
Arnold, F. 407

Balkwill, F. R. 307
Barlow, S. B. 159
Bélanger, P. M. 95
Blagbrough, I. S. 245
Bordin, F. 331

Cabral, F. 159
Cheek, T. R. 173
Cohen, J. S. 211
Colamonici, O. R. 149, 227
Correia, J. J. 127
Court, J. A. 423

Dall'acqua, F. 331
DeLeve, L. D. 287
Donehower, R. C. 35

Fry, D. W. 109
Funato, T. 385

Guiotto, A. 331

Isono, K. 269

Kaplowitz, N. 287
Kashani-Sabet, M. 385
Kingston, D. G. I. 1
Kohn, E. C. 235
Krumwieh, D. 85

Labrecque, G. 95

Na, G. C. 191

Oster, W. 85

Perry, E. K. 423
Pfeffer, L. M. 149, 227

Rowinsky, E. K. 35

Scanlon, K. J. 385
Schulz, G. 85
Stein, C. A. 365

Thomas, H. 307
Timasheff, S. N. 191
Tone, T. 385
Tonkinson, J. L. 365

Usherwood, P. N. R. 245

West, D. C. 407

Yakubov, L. 365

AUTHOR INDEX

Andreu, J. M. 191
Arnold, F. 407

Balkwill, F. R. 307
Barlow, S. B. 159
Bélanger, P. M. 95
Blagbrough, I. S. 245
Bordin, F. 331

Cabral, F. 159
Cheek, T. R. 173
Cohen, J. S. 211
Colamonici, O. R. 149, 227
Correia, J. J. 127
Court, J. A. 423

Dall'acqua, F. 331
DeLeve, L. D. 287
Donehower, R. C. 35

Fry, D. W. 109
Funato, T. 385

Guiotto, A. 331

Isono, K. 269

Kaplowitz, N. 287
Kashani-Sabet, M. 385
Kingston, D. G. I. 1
Kohn, E. C. 235
Krumwieh, D. 85

Labrecque, G. 95

Na, G. C. 191

Oster, W. 85

Perry, E. K. 423
Pfeffer, L. M. 149, 227

Rowinsky, E. K. 35

Scanlon, K. J. 385
Schulz, G. 85
Stein, C. A. 365

Thomas, H. 307
Timasheff, S. N. 191
Tone, T. 385
Tonkinson, J. L. 365

Usherwood, P. N. R. 245

West, D. C. 407

Yakubov, L. 365

SUBJECT INDEX

Acetaminophen, circadian variation in metabolism 103
Acetylcholinesterase inhibitors, effect on dementia 434
N-Acetylcysteine, effect on glutathione levels 299
Actin, calcium and secretion in chromaffin cells 180, 181
Actin-binding proteins, in chromaffin cells 181
Acute lymphocytic leukemia
  vinblastine therapy 46
  vincristine therapy 40
Adenosine analogs, antiviral activity 271
Adhesion molecules
  angiogenesis and wound healing 413
  phosphorothioate oligodeoxynucleotides and expression of 379
  tumor metastasis 237, 239
Adjuvant therapy, IL-3 and GM-CSF 85–94
Adrenal chromaffin cells, calcium signalling and secretion 173–189
Agatoxins 248
Alzheimer's disease 423
  nerve growth factor 435
  neurotransmitter abnormalities 424
  nicotine effects 430
  receptor transmembrane signalling 427
  transmitter augmentation 434
  transmitter replacement 428
Ametantrone
  inhibition of nucleic acid synthesis 113
  interaction with DNA 111
  structure 110
4′-Aminoacyl-4′-deoxypyranosyl cytosines 277
3′-Amino-3′-deoxyadenosine 277
Angelicins
  chemical synthesis 333
  DNA interactions 339
  effect on eucaryotic microorganisms 351
  effect on mammalian cells 346
  natural occurence 333
  photocarcinogenesis 353
  photochemical and photophysical events following irradiation 338
  photoreactions with unsaturated fatty acids 343
  effect on procaryotic microorganisms 350
  protein interactions 344
  skin phototoxicity 345
  therapeutic activity 354
  effect on viruses 352
Angiogenic factors, wound healing 410
Angiogenesis
  tumor metastasis 237, 239
  wound healing 407–422
Angiotensin II, calcium signalling and secretion in chromaffin cells 177
Aniline hydroxylase, in liver, circadian variations 102
Annexins, in chromaffin cells 182
Ansamitocin P-3, tubulin binding 136
Anthracenediones 109
  antiproliferative, cytotoxic and cell cycle effects 114
  DNA interaction 111
  inhibition of nucleic acid synthesis 113
  inhibition of topoisomerase II 115
  mechanism of cell kill 118
  structure 110
Anthrapyrazoles 109
  antiproliferative, cytotoxic and cell cycle effects 115
  DNA interaction 112
  inhibition of nucleic acid synthesis 114
  inhibition of topoisomerase II 115
  mechanism of cell kill 118
  structure 110
Antibiotic nucleosides 269–286
Antimicrotubule agents
  cancer therapeutics 35–84
  chemistry 1–34
Antimitotic agents
  resistance to as genetic probes of microtubule structure and function 159–171
  effect on tubulin–nucleotide interactions 127–147
  tubulin interaction, physicochemical methods of evaluation 191–210
Antioxidant, glutathione 288
Antisense oligodeoxynucleotides 212, 365
  cell-free and model systems 218
  cellular genes 219
  viruses 219
AP-1, cisplatin resistance 388
Aphidicolin, modulation of cisplatin resistance 394
Aptamers 222
1-β-D-Arabinofuranosylcytosine, cisplatin interaction 397
Arachidonic acid, role in exocytosis from chromaffin cells 184
Arachidonic acid metabolites, role in interferon-α signal transduction 154
Arecoline, treatment of Alzheimer's disease 428
Argiopinins 251
Argiotoxins 248, 257
  analogs 259
ArgTX-636 250, 252, 254, 257, 261
Aristeromycin 271
Arthropods, glutamate receptor, venoms and toxins 248
Atenolol, chronopharmacokinetics 96, 97
Autocrine motility factors 239, 241
AZT, cisplatin interaction 396

Baccatin III
  chemistry 10
  sources 6
  structure 2, 4
  structure–activity relationships of analogs 27
  synthesis 18

Bacteria, effect of angelicins 350
Beta-blocking agents, chronopharmacokinetics 96, 97
Bethanecol, effect on Alzheimer's disease 429
Bile, glutathione excretion 295
Biliary excretion, circadian variations 105
Bis(platinum)complexes 392
Blastocidin S 277
Blood flow, circadian variations 98
Bone, wound healing 409
Brain derived neurotropic factor 435
Breast cancer
  angiogenesis 239
  vinblastine 48
  vinorelbine 55
Buthionine sulfoximine
  adjuvant to chemotherapy 299
  modulation of cisplatin toxicity 394

Cachexia, tumor necrosis factor 322
Cadeguomycin 274
Calciosomes 177
Calcium, signalling and secretion in chromaffin cells 173–189
Caldesmon 180
Calmodulin, role in secretion from chromaffin cells 183
Calpactin, in chromaffin cells 182
Cancer
  activity of taxol derivatives 27
  cisplatin resistance 385–406
  effect of integrins and cytokines 307–330
  invasion and metastasis 235–244
Cancer chemotherapy
  antimicrotubule agents 35–84
  hematopoietic growth factors 87
Carbamazepine, circadian variations in distribution 99
Carboplatin 392
Carboxyamido-imidazole 241
Catecholamines, secretion from chromaffin cells, calcium signalling 173–189
Cathepsins B, L and D, role in tumor metastasis 238, 240
Cell adhesion molecules, angiogenesis and wound healing 413
Cephalomannine 4, 5, 15, 16
Chemoattractants, tumor cell migration 238, 241
Chemotherapy
  antimicrotubule agents 35–84
  glutathione 299
  hematopoietic growth factors 87
Chinese hamster ovary cells, tubulin mutants 162
Cholesteryl-linked phosphorothioate oligodeoxynucleotides 374
Cholinergic activities in dementia 424, 425, 428
Chromaffin cells, calcium signalling and secretion 173–189
Chronic lymphocytic leukemia, resistance to intercalators 118
Chronopharmacology 95–105
Circadian rhythms
  drug absorption 97
  drug distribution 99
  drug excretion 104
  drug metabolism 100
Cisplatin, resistance in human cancers 385–406
  circumvention 392
  early detection 391
  exploitation 396
  mechanisms 386
  modulators 393
C-nucleotides 276
Coaristeromycin 272
Colcemid, resistance 163, 168
Colchicine, tubulin interaction 129, 132, 141, 194, 199, 204
Collagenases, tumor metastasis 238, 240
Colony stimulating factors 85
COP-BLAM regimes 41, 42
Cyclic AMP-responsive element binding protein 389
Cyclobut-A(G) 273
Cyclopentenylcytosine 272
Cyclophosphamide, cisplatin interaction 397
Cyclophosphamide–doxorubicin–vincristine 42
Cyclophosphamide–vincristine–prednisone 41
Cyclosporin A, cisplatin resistance 394
Cysteine, storage and transfer 290
Cytochrome P450, in liver, circadian variations 102
Cytokines
  cell regulatory properties *in vitro* 310
  regulation of hematopoiesis 86
  effect on tumors, animal models 308–325
Cytoskeleton, calcium and exocytosis 178

Damage recognition proteins 388
3-Deazaneplanocin A 271
Dementia 423
  neurotransmitter systems 424
  receptor transmembrane signalling 427
  transmitter augmentation 433
  transmitter replacement 428
5′-Deoxytoyocamycin 274
Diacylglycerol, interferon-α induced increase in 151
Dideoxycytidine, cisplatin interaction 396
DNA
  interaction with angelicins 339, 346
  interaction with cisplatin 387, 390, 396
  intercalating antitumor agents 109–125
  strand breaks and cytotoxicity 117
Docosahexaenoic acid, effect on cisplatin activity 393
Dolastatin-10, tubulin interaction 137
Dopamine receptors, in dementia 427
Drug resistance 386
  fos oncogene 388, 395
  tubulin mutants 162
DUP-937, 941 and 942 110

Echiguanines 271
Epidermal growth factor
  role in cisplatin resistance 391
  wound healing 414, 416
Estrogenic drugs, effect on microtubule assembly 134
Etanidazole, cisplatin interaction 397
Etoposide 48
Excitatory amino acids, effect on dementia 432
Exocytosis 173
  calcium 178
  receptor-activated 174
Ezomycin S 281

F-actin 181
Fatty acids, photoreactions with angelicins 343

Fatty acyl nucleosides 280
Fibroblast growth factor, wound healing 410, 417
Fibroblasts, wound healing 409
5-Fluorouracil + cisplatin 397
5-Fluorouracil + interferons 316
Fodrin, role in exocytosis 181, 182
5-Formyloxymethyluridine 275
Fosfadecin 281
Fosfocytocin 281
fos oncogene, drug resistance 388, 395
FR-900403 277
FR0900848 280
Fumagillin, inhibition of tumor growth 239
Furocoumarins 332
  phototoxicity 345

GABA receptors, dementia 426
Galanin 433
Gastric emptying, circadian variation 98
Gelsolin, chromaffin cells 180
Gene expression, sequence-specific inhibition by phosphorothioate oligodeoxynucleotides 377
Gene therapy, interferon-α 314
Gene transcription, effect of phosphorothioate oligodeoxynucleotides 380
Germ cell malignancies, vinblastine 47
Glomerula filtration rate, circadian variation 104
5-*O*-α-D-Glucopyranosyltoyocamycin 277
5-*O*-α-D-Glucopyranosyltubercidin 277
Glucuronidation, in liver, circadian variations 103
Glutamate receptors
  arthropods 248
    polyamine amide toxin interaction 255, 258, 260
  in dementia 427, 432
  vertebrates 247
    polyamine amide toxin interaction 250, 254, 259, 260
Glutathione
  circadian variation 103
  detoxification by 288
  efflux from liver 294
  interorgan homeostasis 296
  mitochondrial 292
  role in cisplatin resistance 387, 394
  structure 287
  synthesis 293
  therapy 299
  thiol–disulfide exchange 290
  tissue distribution 291
Glutathione *S*-transferases, function 297, 298
Glycosyl nucleosides 277
Granulocyte-macrophage colony-stimulating factor
  clinical effects 87
  combination with interleukin-3 90
  molecular biology and function 86
Griseolic acids 280
Growth hormone, wound healing 414
Guanine nucleotides, tubulin interactions 128–147
Guanine 7-*N*-oxide 270
Guanosine analogs 275

H-7, modulation of cisplatin cytotoxicity 393
Hematopoietic growth factors, adjuvant therapy 85–94
Herpes simplex virus, effect of phosphorothioate oligodeoxynucleotides 376
Het toxins 258
Hexobarbital, circadian variation in metabolism 101
Histamine, calcium signalling and secretion in chromaffin cells 177
HIV
  effect of nucleoside antibiotics 270–274
  effect of oligonucleotides 218, 369
Hodgkin's lymphoma
  vinblastine treatment 47
  vincristine treatment 40
Hydantocidin 276
5-Hydroxymethylblasticidin S 277

Indole nucleosides 276
Indomethacin, chronopharmacokinetics 96
Inflammation, wound healing 408, 413
Informational drugs 211, 222
Ins(1,4,5)P_3-mobilizing hormones, calcium signalling and secretion in chromaffin cells 177
Integrins, tumor metastasis 237, 240
Interferon-α
  antitumor effects in animals 312
    combination with interleukin-2 319
  chemotherapy 316
  clinical studies 314
  transmembrane signalling 149–157
Interferon-α receptor 227
  binding studies 231
  cDNA cloning 230
  immunoprecipitation 231
  structure 228
Interferon-β, antitumor effects in animals 315
  combination with interleukin-2 319
Interferon-γ
  antitumor effects in animals 315
    combination with interleukin-2 319
    combination with tumor necrosis factor 323
  clinical studies 316
Interferon-stimulated gene factors 153
Interferon-stimulated genes 153
Interferon stimulus response element 153
Interleukin-1
  antitumor activity in animals 317
  induced ICAM-1 379
Interleukin-1β gene, effect of phosphorothioate oligodeoxynucleotides on production of 379
Interleukin-2
  antitumor activity in animals 317
    combination therapy 319, 324
  clinical studies 320
Interleukin-3
  clinical effects 88
  combination with GM-CSF 90
  molecular biology and function 86
Interleukin-4, antitumor activity in animals 320
Interleukin-6
  antitumor activity in animals 320
  clinical correlates 321
Interleukin-11 92
Intracellular adhesion molecule-1, effect of phosphorothioate oligodeoxynucleotides on expression of 379
Invasion and metastasis
  clinical significance 235
  Diagnostic and therapeutic potential 239
  process of 236
Iproplatin 392

Joro spider toxins 250, 252, 254, 256, 257
  analogs 259

Kainate-sensitive receptor 247
Kaposi's sarcoma, vinblastine 49
3′-Ketoneplanocin A 271
Ketoprofen, chronopharmacokinetics 97, 98
Kidney
  chronobiology 104
  glutathione and detoxification 291

Laminin receptor, tumor metastasis 237, 239
α-Latrotoxins 248
Leukemia
  granulocyte-macrophage colony-stimulating factor 87
  vinblastine therapy 46
  vincristine therapy 40
Leukotrienes, glutathione and metabolism of 288
Lewy body dementia
  neurotransmitter abnormalities 424
  neurotransmitter augmentation 434
Lipids, effect of interferon-α on metabolism 151
Lipocortin, in chromaffin cells 182
Liver
  biological rhythms in drug metabolism 100
  glutathione efflux 294
  glutathione metabolism and detoxification 291
Lung, glutathione and detoxification 291
Lung cancer, vinorelbine 55
Lymphoma
  effect of granulocyte-macrophage colony-stimulating factor 87
  vinblastine treatment 47
  vincristine treatment 40
Lymphotoxin 321

Maytansin, tubulin biding 136
Metallothioneins, cisplatin resistant cells 387
Metastasis
  animal models 311
    effect of interferons 314, 316
  clinical significance 235
  diagnostic and therapeutic potential 239
  process of 236
  vinblastine 48, 49
  vincristine 42
Methylangelicins
  photolysis under UVA excitation 338
  synthesis 335
  therapeutic activity 354
N-Methyl-D-aspartate receptor 247
  in dementia 427, 432
  polyamine amide toxin interaction 252, 255, 259, 262
3-Methylpseudouridine 276
Microtubule associated proteins 139
  interaction with antimitotic drugs and nucleotides 141
Microtubule organizing centres 128, 159
Microtubules 128
  antimitotic drugs as genetic probes of structure and function 161–170
  assay of taxol derivatives 26
  distribution 159
  drug inhibition of assembly 130
  dynamic properties 160
  thermodynamic linkage 131
  vinca alkaloid interaction 37
Mildiomycin 277
Mitochondria, glutathione in 292

Mitoxantrone
  antiproliferative, cytotoxic and cell cycle effects 114
  inhibition of nucleic acid synthesis 113
  inhibition of topoisomerase II 115
  interaction with DNA 111
  structure 110
MOF 42
Monoamines, effect on dementia 432
Monoclonal antibodies, interferon-α receptor 229
MOPP 40, 47
Multidrug resistance, oligodeoxynucleotides 220
Mureidomycins 279
Muscarinic agents, effect on dementia 429
Mycalisines 275
Mycosis fungoides, angelicins 355

Neosidomycin 276
Neovascularization, wound healing 408
Nephila spider toxins 250, 257
Neplanocin A 271
Nerve growth factor, therapy in Alzheimer's disease 435
Neural implantation, dementia 436
Neurotransmitter systems in dementia 424
Neurotropin-3 435
Neutropenia, effects of granulocyte-macrophage colony-stimulating factor 87
NG-*k*B 155
Nicotinic acetylcholine receptors, polyamine amide toxins 254
Nicotinic-cholinergic therapy, dementia 429
Nikkomycins 278, 280
p-Nitroanisole *O*-demethylase, in liver, circadian variations 100, 102
Non-small cell lung cancer, vindesine 51
Nucleoside antibiotics 269–286
Nucleotide antibiotics 281

Octosyl acids 280
Oligodeoxynucleotide binding protein 215
Oligodeoxynucleotides 211, 365
  antisense applications 218
  aptamers 222
  cellular uptake 216
  inhibition of polymerase 221
  phosphorothioate 365–384
  properties 214
  ribozymes 222
  synthesis 213, 366
  therapeutic considerations 222
  triplex formation 221
Ovarian cancer
  taxol 61
  vinorelbine 55
Oxalatoplatin 392
Oxetanocin analogs 272
Oxidant stress, role of glutathione 288
L-2-Oxothiazolidine-4-carboxylate 299

p70, in chromaffin cells 182
Pacidamycins 279
Parkinson's disease
  neurotransmitter abnormalities 424
  neurotransmitter augmentation 434
Peptidyl nucleosides 278
Phalloidin 181
α-Philanthotoxin 249

analogs 258
interaction with glutamate receptor 253, 254, 256, 261
Phomopsin A, tubulin interaction 137
Phospholipase A2, role in exocytosis 184
Phosmidosine 281
Phosphorothioate oligodeoxynucleotides 365
anti-viral agents 369
pharmacology 369
physicochemical properties 366
regulation of gene transcription 380
sequence-specific inhibition of gene expression 377
Photocarcinogenesis, angelicins 353
Photohemolysis, angelicins 349
Photolysis of angelicins 338
Phototoxicity, angelicins 345
Physostigmine, therapy in dementia 434
Plasma cell dyscrasia, vincristine 42
Plasminogen activators, tumor metastasis 238, 240
Platelet-derived growth factor, role in cisplatin resistance 391
Platelet lysates, wound healing 417
Platinum(II) antitumor agents 392
Podophyllotoxin, binding to tubulin 132, 133
Polyamine amide toxins 246, 248
action on glutamate receptors 250, 260
isolation and characterisation 249
mode of action 260
pseudo-hybrid analogs 259
structure–activity relationships 256
synthetic 258
Polymerase chain reaction, assay of cisplatin resistance 391
Polymerases, inhibition by oligonucleotides 221
Post-irradiation dark hemolysis 349
Propranolol, chronopharmacokinetics 96, 97
Psoralens, angelicins 332
Psoriasis, therapeutic activity of angelicins 354
Proteinases, tumor metastasis 238, 240
Protein kinase C
in chromaffin cells 183
interferon-α activation of 151, 154
role in cisplatin resistance 390, 393
Protein self-association, tubulin-drug binding 192, 200
PUVA 332
Pyrrolosine 276

Quisqualate-sensitive receptor 247
polyamine amide toxin interaction 250, 255, 258, 261

Rhizoxin, tubulin binding 136
Rhythms, drug metabolism 95–107
Ribozymes
gene expression and drug resistance 395
oligonucleotides 222
RS 86, effect on Alzheimer's disease 429

Salicylate, circadian variation in excretion 105
Sangivamycin 274
Scinderin 181
Selegiline 435
Serum responsive elements 389
SF-2140 276
Signal transduction
cisplatin resistance 388, 394
interferon-α 150
Skin cancer, angelicins 354
Skin phototoxicity, angelicins 345
Small cell lung cancer, vincristine 42
Sotalol, chronopharmacokinetics 96, 97
Spider toxins 246, 248
action on glutamate receptors 250
analogs 259
isolation and characterization 249
Staurosporine, effect on transmembrane signalling by interferon-α 154
Stem cell factor 92
Subtilisin 134
Sulfate conjugation, in liver, circadian variations 103
Synexin, in chromaffin cells 182

Taxanes
bioactivity 26
biosynthesis 24
cancer chemotherapy 56
sources 4
structure 4
Taxol 1–34, 56–65
biosynthesis and biotransformation 24
chemistry 10
clinical pharmacology 58
clinical trials 59
isolation and structure 3, 139
mechanism of action 56
NMR spectra 7
preclinical antineoplastic activity 57
resistance 58, 163
sources 4
structure–activity relationships of derivatives 26
synthesis 18
toxicities 62
tubulin interaction 129, 138, 142, 161
Taxotere 7, 30, 32
antineoplastic activity 65
X-ray structure 10
Taxusin, synthesis 21, 23
Testosterone, temporal variations in hydroxylation 102
Tetrahydroaminoacridine, therapy in dementia 434
Tetraplatin 392
Theophylline, chronopharmacokinetics 97, 98
6-Thioguanosine 275
Thiol–disulfide exchange, glutathione 290
4-Thiouridine 276
Thrombopoiesis, interleukin-3 and granulocyte-macrophage colony-stimulating factor 86
Topoisomerase II
inhibition by anthracenediones and anthrapyrazoles 115
role in intercalator induced cytotoxicity 117
Toyocamycin 274
Toyocamycin glucopyranoside 277
Transcriptional activation, interferon-α 153
Transcription factors, cisplatin resistance 389
Transgenic mice, effect of cytokines 312
Translation arrest, oligonucleotides 211, 212
4,6,4′-Trimethylangelicin 355
Triplex formation, oligonucleotides 221
Tubercidin glucopyranoside 277
Tubulin
antimitotic drug interactions 129, 161, 192
colchicine binding 132, 194, 199, 204
dolastatin 10 binding 137
maytansinoid binding 136

measurement of ligand binding 195–208
mutants in mammalian cells 162
N-site GTP 140
nucleotide interactions 128–147
phomopsin A binding 137
podophyllotoxin binding 132, 133
protein self-association 192, 200
taxol derivatives 27, 28
thermodynamics of binding reactions 204
third nucleotide binding site 140
vinca alkaloid binding 37, 135, 193, 203
Tumor necrosis factor
antitumor activity in animals 321
cachexia 322
clinical correlates 324
combination therapy 323
Tumors
effect of cytokines in animal models 308–325
invasion and metastasis 235

Unsaturated fatty acids, photoreactions with angelicins 343
Uridine analogs, antibiotic activity 275
Urologic malignancies, vinblastine 47
UVA, photolysis of methylangelicin 338

Vinblastine
clinical pharmacology and applications 46
structure 36
toxicities 49
tubulin binding 135–138, 141, 193, 203
Vinca alkaloids 36
tubulin binding 135
resistance 37
Vincristine
clinical applications 40
clinical pharmacology 38
dose and schedule 39
resistance 37, 43
structure 36
toxicity 43
tubulin binding 135, 141
Vindesine 36
clinical pharmacology 50
clinical trials 51
toxicities 52
Vinorelbine 37
clinical pharmacology and trials 54
preclinical 53
toxicity 55
Viruses
effect of angelicins 352
antisense oligonucleotides 219, 369
nucleoside antibiotics 269–286

Wasp toxins 246, 248
analogs 258, 260
glutamate receptor interactions 253
isolation and characterization 249
Wound healing, angiogenesis 407–422

Yeast, effect of angelicins 351
Yew, taxanes 2

Xeroderma pigmentation binding factors 388
X-irradiation, cisplatin resistance 394